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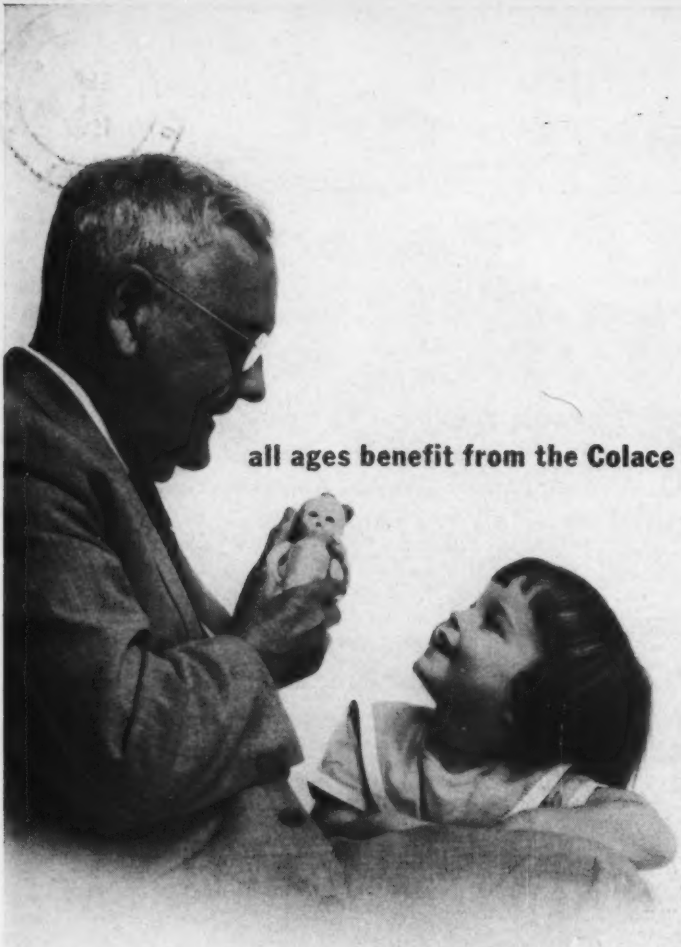

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OF THE CHILDREN'S HOSPITAL

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SUBDIAPHRAGMATIC ABSCESS IN INFANTS AND CHILDREN

Gloria Eng, M.D.,* Walter E. Ahrens, M.D.†

In July, 1949, a 2 year old child was admitted on 2 occasions to the Children's Hospital of D. C. with a complaint of unexplained fever. Subsequently, at another hospital a metastatic subdiaphragmatic abscess was recognized after an additional 3 weeks of study. That child finally recovered, and the case was reported[1]. The total hospital course extended over 3 months. Recently, a 4 year old child was referred to Children's Hospital from another hospital with unexplained fever and chest pain. The physician who had cared for the first child immediately recognized the possibility of a subdiaphragmatic abscess in the second child. The prompt correct diagnosis and early adequate treatment permitted this second child to be discharged 15 days after admission, entirely well.

Admittedly, subdiaphragmatic abscesses are uncommon in children, often present vague and non-localizing signs for some time, and may be masked or delayed by antibiotic therapy. Nonetheless, with the above experience in mind, the authors wish to present a case report, to summarize the 9 cases treated at this hospital in the past 20 years, and to review the pertinent literature concerning subdiaphragmatic abscesses in infants and children.

CASE REPORT

A. L., a 4-year-old white girl, was admitted to Children's Hospital in November 1956 with intermittent fever for 2–3 months and left chest pains for 16 days.

She was well until 3 months before admission when multiple furuncles of the arms and trunk developed and persisted for 3 weeks. They were not treated medically. Two and one-half months before admission the onset of anorexia, listlessness, constipation, vague lower abdominal pains, and intermittent fever were noted. One week later the child contracted chickenpox. Two months before admission, pain referral shifted from the abdomen to the low back.

Seventeen days prior to admission to Children's Hospital the child entered a Maryland hospital for study of these complaints. Tuberculosis was seriously considered. A kidney infection was diagnosed on the basis of pyuria and slight hematuria. One day later, pain was localized to the left chest. The child was discharged after 5 days on oxytetracycline and isoniazid therapy. Subsequent to this, left chest pain continued especially with respiratory movement. The left shoulder was consistently tilted below the level of the right shoulder. Pain and swelling of the lower left chest and upper abdomen were observed 8 days before referral. Five days before admission a cough productive of brown mucoid sputum was noted.

When seen in the Out Patient Department the child was admitted to the isolation ward with a diagnosis of tuberculous pneumonia.

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Six siblings and both parents were well. No immunizations had been given. Growth and development prior to this illness were described as normal. Of possible significance in this child's illness was the history of a positive patch test to tuberculosis at the age of 2 years, a contact with tuberculosis, and an environment which included exposure to chicken housing on a southern Maryland farm.

On physical examination vital signs were a rectal temperature of 98 degrees, pulse of 100 per minute, respirations 25 per minute, and blood pressure of 100/60. She was a pale, irritable, chronically ill, white girl in no acute distress. Significant findings included the following: A boggy nasal mucosa with mucous discharge, a yellow postnasal discharge, an apparent fullness of the left lateral and anterior chest and upper abdomen with a distended venous pattern over this area, accompanied by tenderness to percussion and dullness to percussion of the lower one-third of the left anterior and posterior chest and flatness to percussion over the lower one-half of the left lateral chest with markedly decreased breath sounds of this area, but no rales in any part of the chest; there was no cardiac murmur or arrhythmia, the liver was palpable

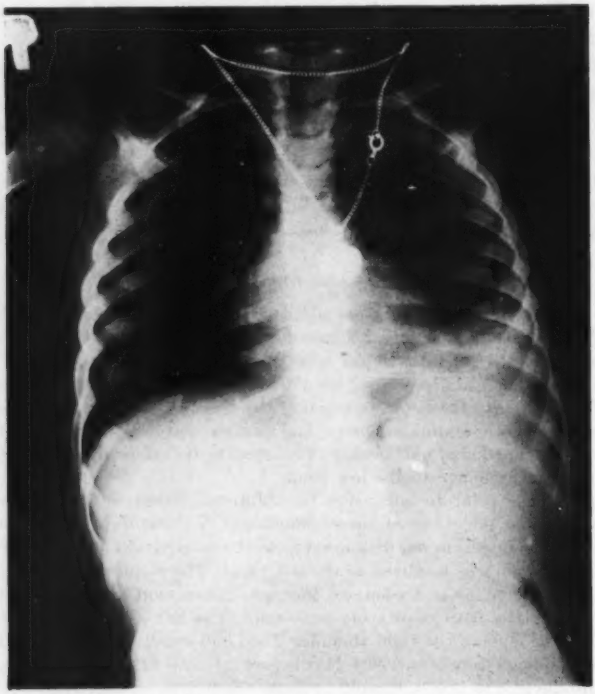

FIGURE 1. Roentgenographic examination of the chest in the anterior-posterior view: Note an area of infiltration overlying the left diaphragm having the appearance of an inflammatory process. Fluoroscopy revealed a fixed left diaphragm.

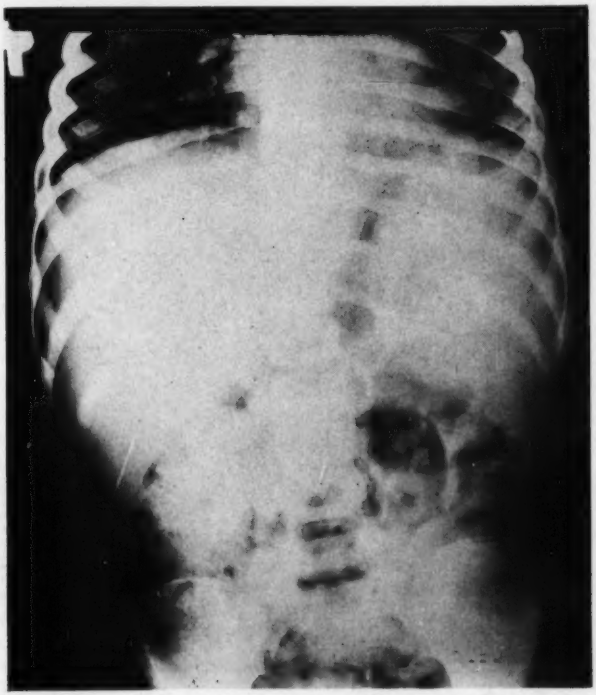

FIGURE 2. Flat plate of the abdomen revealing a mass which displaced the stomach medially.

1–2 cm below the right costal margin and the spleen was questionably palpable. The remainder of the physical examination was unremarkable.

Complete blood count revealed a hemoglobin of 9.4 gm per 100 ml, hematocrit of 33 per cent, a white blood count of 13,900 per mm with 67 per cent segmented forms, and 1 per cent band neutrophiles, 1 per cent eosinophiles, 25 per cent lymphocytes, and 6 per cent monocytes, and a smear showing slight microcytosis, anisocytosis, and a rare target cell. Urine showed a specific gravity of 1.022, a trace of protein, and 7–9 white blood cells per high power field, 1–2 red blood cells per high power field, and no casts. Sedimentation rate corrected was 46 mm per hour. Intermediate tuberculin and histoplasmin skin tests were negative at 48 hours. Blood urea nitrogen was 9.5 mg per 100 ml. Nasopharyngeal and blood cultures were negative.

The clinical picture was suggestive of a possible left subdiaphragmatic abscess. Fluoroscopy and antero-posterior and lateral chest x-rays revealed an elevated and fixed left diaphragm, a subdiaphragmatic density compressing the stomach medially and anteriorly, and an infiltration in the left lung base. Intramuscular pyelogram

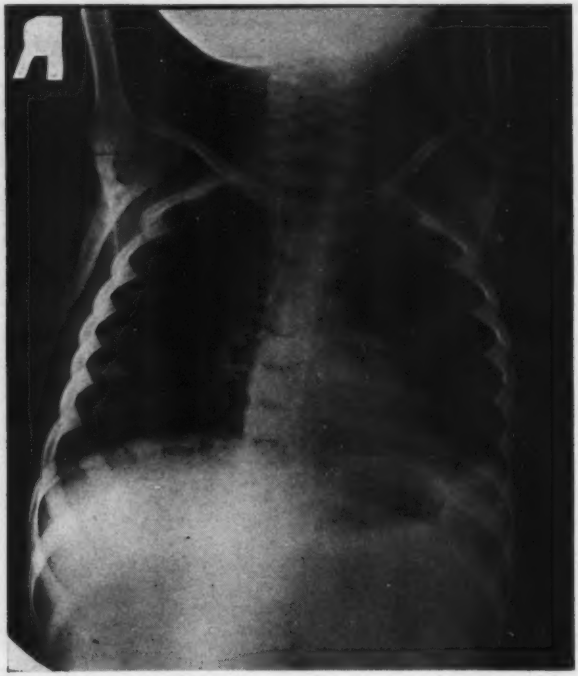

FIGURE 3. Postoperative roentgenogram: The pathology previously reported in the left lower chest has undergone almost complete resolution. The stomach has shifted back to a more normal lateral position.

demonstrated prompt dye excretion and no distortion. There was displacement of the left renal calyces downward and medially.

On the basis of the clinical impression and x-ray evidence, a left subdiaphragmatic abscess and an associated sympathetic pneumonia of the left lower lobe were considered to be present. Surgery was performed on the fifth hospital day and an abscess was drained from beneath the left diaphragm by the intraperitoneal route. No evidence of an intra-abdominal focus of infection such as an infected appendix could be found. Hemolytic staphylococcus aureus was cultured from the pus and was sensitive only to chloramphenicol, erythromycin, and carbomycin.

Post-operatively the course was uncomplicated. The only fever observed during the entire hospital stay was on the first post-operative day. The antibiotics used in therapy were penicillin and chloramphenicol. On the second post-operative day the child was eating a soft diet and was sitting up. By the fifth post-operative day she was out of bed. On the tenth post-operative day the chest inflammation had almost completely resolved, and the child was discharged.

Biographical Data

Sex	Male 5	Female 4
Color	White 5	Negro 4
Age Range	18 months–12 years	
Age Distribution	0 to 4 years	3
	4 to 8 years	2
	8 to 12 years	4

Predisposing Cause

Post-operative		6
Appendicitis with perforation	4	
Repair of lacerated liver	1	
Splenectomy in leukemia	1	
Metastatic		3
Pyoderma	1	
Tonsillitis	1	
Unknown focus	1	

Etiologic Organism (from Abscess)

Post-operative: *Staphylococcus aureus* 1, *Staphylococcus albus* 1, Hemolytic streptococcus 1, *Escherichia coli* 1, *Proteus vulgaris* 1, Unknown 1

Metastatic: *Staphylococcus aureus* 1, *Staphylococcus albus* 1, Hemolytic streptococcus 1

Symptoms

Fever	9
Anorexia	5
Abdominal pain	5
Cough	4
Vomiting	4
Chest pain	2
Loose stools	2
Rhinorrhea	1
Sore throat	1
Listlessness	1

Signs

Chest:	
Dullness to percussion	5
Local fullness	3
Decreased breath sounds	3
Tachypnea	2
Local tenderness	1
Rales	1
Brown sputum	1
Abdomen:	
Local tenderness	4
Local fullness	3
Palpable mass	1
Local rigidity	1
Hepatomegaly	1
Persistent wound discharge	1

Signs (Continued)

Skin:		
Local venous pattern distended		1
Pallor		1
Yellow skin		1
Tarry stool		1

Laboratory Data

Anemia (hemoglobin below 10 Gm per 100 ml)		7
Leukocytosis (above 12,500 WBC/mm³)		9
Blood cultures:		
Positive		1
Negative		2

Roentgenographic Findings

Abnormal Chest X-ray		9
Elevated diaphragm	9	
Infiltration in lung base above diaphragm	8	
Fixed diaphragm	6	
Density under diaphragm	3	
Fluid in costophrenic angle	3	
Displaced abdominal organs	3	
Air under diaphragm	2	

Admitting Diagnoses

Infectious hepatitis, pneumonia, tuberculous pneumonia, pharyngitis, pyelonephritis, poliomyelitis

Location of Subdiaphragmatic Abscess

Left side (associated with perforated appendix 2)	4
Right side (associated with perforated appendix 2)	5

Complications Associated

Metastatic	None
Post operative:	
Recurrence of subdiaphragmatic abscess	4
Appearance of other intra-abdominal abscesses	1
Adhesions, fistula, and intestinal obstruction	1
Osteomyelitis of 12th rib	1
Pneumohydrothorax	1
Mortality	1
(Leukemia with recurrence of subdiaphragmatic abscess complicating splenectomy)	

Speed of Diagnosis

	Metastatic	Post Operative
Time period		
Onset of symptom to hospital admission	1 day to 2½ months	4 days to 3 weeks
Admission to roentgenographic diagnosis	3 days to 10 days	9 days to 4 weeks
Admission to operative drainage	5 days to 7 weeks	12 days to 6 weeks

COMMENT

Information on 9 cases of subdiaphragmatic abscess seen at Children's Hospital between 1936–1956 is included in the accompanying tables, most of which are self-explanatory. That subdiaphragmatic abscesses in children are uncommon is apparent by the paucity of cases seen in a 20 year period of pediatric surgery in a large pediatric hospital.

In this small series there was no significant age, sex, or color distribution. The most common predisposing cause was a ruptured appendix, and nearly as common was metastasis from a distant focus of infection.

An organism was isolated from the abscess in 8 of 9 cases and yet was Gram negative in only 2. All 3 of the metastatic subdiaphragmatic abscesses were caused by Gram positive cocci. This would seem an observation of value in considering appropriate antibiotic therapy.

The signs and symptoms recorded include those in the post-operative group after initial surgery. Fever, anorexia, vague or localized abdominal pain, and cough were the most common symptoms. Local chest and abdominal signs including the observation of local fullness or bulging of the chest or abdominal wall were signs of greatest value.

Laboratory evidence was consistent with infection in all cases. In every case roentgenographic examination eventually confirmed or created the clinical diagnosis. Fluoroscopy was of particular value in several cases. Either lagging or elevation and fixation of a diaphragmatic leaf was consistently the earliest sign of a developing abscess.

In contrast to common belief, in this series there was no significant difference in the incidence of left and right sided abscesses. Two left and two right sided abscesses occurred in association with perforated appendices.

All but 1 of these 9 children received 1 or several antibiotics, and there was no apparent correlation of the type of antibiotics with the clinical course or type of complication. Five of these 9 children were treated during the past 8 years when a variety of antibiotic agents was available.

The most striking feature of the subdiaphragmatic abscess in these children was not the mortality rate but rather the incidence of severe complications and prolonged hospital course. The shortest hospital course was the present case report of 15 days. Eight patients were hospitalized for over a month, and 5 patients were hospitalized from 2½ to 4 months.

DISCUSSION

Historically, the earliest description of a subdiaphragmatic abscess was recorded in an isolated case observed at autopsy in 1826 by Louis[2] of France. Barlow[3] in 1845 described a case of a perforated stomach associated with obscure thoracic symptoms. Shortly thereafter, Maydl's[4] mono-

graph on the subject appeared. In 1898 Martinet's[5] detailed anatomical treatise on the variations of the subdiaphragmatic abscess stimulated Barnard[6] in 1908 to elaborate further on the anatomic spaces and their surgical implications. Ochsner[7] and his co-workers have set the pattern in recent years for the recognition and management of this uncommon infection. Further study on recent variation in pattern and location of subdiaphragmatic abscesses has been performed by Gerwig and Blades[8], who urge re-evaluation of this condition in our antibiotic era.

In examining reported series of patients with subdiaphragmatic abscesses, it is interesting and important to note that although the majority of cases occur in adults, children are by no means exempt. Brown[9] reported 4 cases in children. Ireland[10] presented 6 cases ranging from 14 months of age to 12 years of age. Anspach[11] emphasized the roentgenographic changes in 10 children. Ochsner, et al.[12] in their own collection had 13 cases, the ages varying from 9 to 19 years. Faxon[13] reported a series of 111 consecutive cases in which there were 6 patients between the ages of 3 and 10 years, and 12 patients between the ages of 10 and 20 years. Ladd and Swan[14] had a series of 14 patients under 11 years of age, and 6 of these were under 2 years of age. In a series of 154 patients reviewed by Berens et al[15], ages ranged from 3 to 77 years of age, but the number of children was not stated. Heidenblut[16] described an 8 day old infant with a subdiaphragmatic abscess which was considered to have been an extension of a probable phlebitis of the umbilical vein with the formation and rupture of a subcapsular liver abscess. Another subdiaphragmatic abscess in a young infant was presented by Bentley[17]. In this case there was drainage of a 10 day old infant's abscess into an umbilical sinus producing an umbilical fecal fistula, which appeared externally like an umbilical hernia.

A common etiologic factor of the subdiaphragmatic abscess in the adult is either perforation of a duodenal or stomach ulcer or biliary tract disease. The most common cause in children, however, is a ruptured appendix, which may produce a subdiaphragmatic abscess by any of the following routes: 1) as the result of a generalized peritonitis, 2) as the result of the rupture of a liver abscess secondary to a thrombophlebitis, or 3) as the result of an infection ascending by the paracolic gutter. If the appendix is retrocecal or under the liver, the possibility of spread of infection to the subdiaphragmatic space is increased[18]. Other widespread intra-abdominal suppurative processes causing subdiaphragmatic abscesses as described by Ladd[14] include: 1) primary peritonitis with empyema and septicemia, 2) peritonitis secondary to a ruptured ileum, and 3) septic thrombophlebitis of the umbilical vein with peritonitis. Anspach[11] listed minute perforations of the intestines following either diarrhea, intussusception, or Meckel's diverticulitis as a frequent cause of this condition in

children. Trauma and post operative infections have also been implicated as known causes of subdiaphragmatic abscesses in childhood.

A perinephric abscess or a thoracic empyema may penetrate into the subdiaphragmatic space. Perforation of the stomach, duodenum, or gall bladder, rupture of a liver abscess, and osteomyelitis of thoracic vertebrae or lower ribs are unusual causes of this entity in childhood.

The most difficult subdiaphragmatic abscess to diagnose promptly and correctly is the metastatic abscess, in contrast to the more common, aforementioned, contiguously spreading infections. This type of abscess may follow weeks or months after a vague upper respiratory infection, otitis media, furunculosis, or distant osteomyelitis[14], and is undoubtedly the sequella of hematogenous dissemination of infection.

Harley[19] analyzed the mode of spread of infection from distant areas of the abdominal cavity to the subdiaphragmatic space. He concluded that infected peritoneal fluid within the cavity shifts, stagnates, gravitates to the dependent area when the patient is recumbent and rises by hydrostatic pressure when the patient is upright, to reach the subdiaphragmatic space. Once the infected fluid extends to a part of the diaphragm, the constant movement of the diaphragm and related viscera spreads the fluid over the surface of the liver. The less common mode of spread is via the portal vein. In no case did he note anything to suggest lymphatic spread.

The common organisms incriminated in the formation of a subdiaphragmatic abscess include the streptococcus, the staphylococcus, and *Escherichia coli*, which frequently produces gas resulting in characteristic roentgenographic patterns. Gerwig and Blades[8] found the staphylococcus to be a frequent offender. Parasites such as *Endamoeba histolytica* or the Echinococcus on rare occasion may produce a subdiaphragmatic abscess secondary to rupture of a liver abscess.

The clinical picture may vary with the age of the patient, the etiology of the infection, the location of the abscess, and the duration of illness. For example, in Ladd's[14] patients in whom the abscess was merely part of a widespread intra-abdominal infection, the finding of the abscess was only incidental at autopsy. These patients were all overwhelmingly ill with fever, prostration, vomiting, diarrhea, and abdominal tenderness. In patients with abscesses complicating ruptured appendices, perforation of other viscera, or following surgery for any cause, the symptoms often appear to be gradual exacerbation of the primary disease. There is low-grade or intermittent pyrexia at a time when the patients should be well on the road to recovery. There is unexplained malaise, tachycardia, anorexia, and vague abdominal discomfort. Then cough, dyspnea, pain and tenderness in either the right or left upper abdominal quadrant ensue. Hiccoughing may or may not be present. Edema in the area of the lower axilla has been de-

scribed[20]. Gerwig and Blades[8] cited cases in adults where the first evidence of a subdiaphragmatic abscess in patients receiving antibiotic therapy was a sudden catastrophic accident in which the abscess ruptured into the thoracic cavity producing sudden collapse and a shock-like state.

The metastatic abscess often reveals its presence more insidiously. The symptoms are mild and vague. There is low-grade fever, mild malaise, loss of appetite with subsequent weight loss, pallor, attacks of abdominal pain, chills, sweats, nausea, vomiting, and a dull ache in the region of the abscess. Pulmonary symptoms become more pronounced as weeks and then months elapse, until the diagnosis is finally made. Anspach[11] advises that any child who develops sudden onset of a productive cough with sputum of fetid or mousy odor should be considered to have a possible subdiaphragmatic abscess. Carter[21] observes that pain referred to shoulder and neck is more prominent in left subdiaphragmatic abscesses because of the less-fixed diaphragm. Occasionally jaundice may be associated with a subdiaphragmatic abscess[18].

Physical examination may reveal either a chronically ill or an acutely ill child with anxious expression, flushed facies, warm moist skin, and hacking cough. The patient may lie in bed favoring the affected side; there may be absence of motion and spasm of the abdominal wall musculature of the involved side. A mass may be palpable on the lower chest wall anteriorly or posteriorly, and the liver may be displaced downward. Dullness to flatness on percussion of the chest with splinting of the affected side may be present. In addition, there may be decreased breath and voice sounds, and rales present on auscultation of the involved lung base. Hochberg[18] states that a friction rub may be heard at the lower part of the chest due to the diaphragm rubbing against the upper surface of the liver. A peculiar clicking quality of the second heart sound at the apex may be heard when the left side is involved[18]. Persistent tenderness over the right twelfth rib in postero-superior abscesses is a common and early sign according to Ochsner[12]. Tenderness varies, however, with the location of abscess.

Laboratory aids to the diagnosis are rather non-specific except for roentgenographic studies. There is usually leukocytosis, a moderate or marked anemia, and an increased sedimentation rate. According to Blades[22] antibiotics may mask a subdiaphragmatic abscess and lull the unwary physician by a normal leukocyte count.

The first and most prominent sign on roentgenographic study is elevation and fixation of the diaphragm on the involved side. This is particularly well visualized on fluoroscopic examination and is best demonstrated by contrast when on deep inspiration the uninvolved diaphragm is depressed[11, 12, 14, 18]. The next sign, as abscess formation progresses, is an

adhesive pleuritis on the affected side visualized as haziness with obliteration of the costophrenic angle by fluid. Anspach[11] notes that occasionally loculations develop between two layers of the pleura causing the formation of a convex upper border that may be mistaken for the diaphragm. A late sign according to Ochsner[12] is air formation under the diaphragm with pleural effusion.

The so-called gas and fluid level may be readily visualized by roentgenography in 3 positions, antero-posterior erect, lateral erect, and antero-posterior lateral recumbent. One may readily observe the shifting gas collection below the diaphragm[23].

Displacement or distortion of the stomach bubble by a dense shadow with evidence of diaphragmatic pleuritis is suggestive of left subdiaphragmatic abscess. Carter[21] stresses the fact that in a left subdiaphragmatic abscess the infection is surrounded by more yielding structures, and, hence, there is less elevation and fixation of this portion of the diaphragm. As a result, recognition of a left subdiaphragmatic abscess is often delayed. Carter[21] delineates the left subdiaphragmatic abscess further by roentgenograms following a barium meal. Normally, in Trendelenberg position, the stomach lies directly in contact with the diaphragm. Separation of the barium filled stomach by a space with medial downward displacement of the stomach is strongly suggestive, therefore, of a left subdiaphragmatic abscess. The barium swallow may also eliminate confusion caused by loops of bowel that may give the appearance of free air under the diaphragm.

Diagnostic aspiration of the abscess, except when visualized directly during surgery, is generally agreed to be unreliable and dangerous. Contamination of the pleura is to be avoided.

Zaslow and Sachs[24] believe that the prophylactic use of antibiotics has reduced the incidence of subdiaphragmatic abscess and has often aborted frank suppuration. Once the diagnosis of subdiaphragmatic abscess is considered, adequate antibiotic therapy and good, general, supportive care should be instituted. After pus has formed, however, all writers agree that surgical drainage is essential. The extraserous approach is preferred as the surgical route of choice rather than either transperitoneal or transpleural routes in the evacuation of the abscess[1, 12, 14, 18, 23]. In one adult series the staphylococcus was a frequent infecting organism and in all such reported cases was sensitive to chloramphenicol[22]. Certainly antibiotic therapy would seem indicated in conjunction with surgery, but appropriate change of therapy may be dictated on the basis of antibiotic sensitivities of the organism cultured from the blood or the abscess.

The complications of subdiaphragmatic abscesses are several. Vasomotor collapse due to septic shock may occur in subdiaphragmatic abscess even in the presence of antibiotic therapy[7]. Furthermore, the abscess may rup-

ture into the peritoneal cavity, into one of the viscera, through the skin, or into the thorax. In the latter state, pleural effusion, empyema, bronchopleural fistula, lung abscess, mediastinitis, or pericarditis may ensue. The prognosis in such a case is grave.

CONCLUSION

From this presentation of a case of a metastatic abscess of the left subdiaphragmatic area in a 4 year old child, summary of 9 cases of subdiaphragmatic abscess in infants and children, and a review of the pertinent literature it is apparent that earlier diagnosis and earlier therapy will result in reduced mortality and morbidity.

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HEMOGLOBIN S-C DISEASE

Carlos S. Berrocal, M.D.*

In recent years an increasing number of cases of what had been presumed to be mild sickle cell anemia or sickle cell trait have been identified as hemoglobin S-C disease.

The importance of the accurate diagnosis of the different sickle cell variants rests on the difference in prognosis and treatment as well as on the possibility of genetic counseling.

CASE 1

P. H., a 4 year old negro girl, was first seen in the Out Patient Department at 3 years of age with the complaint of enlarged abdomen and delay in development. Examination then revealed fever and otitis media. The spleen was described as palpable 1.5 cm below the costal margin. Laboratory work at that time revealed 90 per cent sickling. The hemoglobin was 12.1 gm per 100 ml, and the hematocrit 34 per cent. There was also a leucocytosis with a normal differential. The erythrocytes were described as slightly hypochromic. There were many target cells present.

From that time until the present admission she was seen numerous times with the complaints of indefinite abdominal and joint pains.

At the present hospitalization she complained of severe pain in the legs and abdomen which caused her to limp, and fever. Two weeks prior to admission she had had a mild upper respiratory infection.

On admission the patient had a low grade fever and a moderate amount of lymphoid hyperplasia of the pharynx. The spleen was palpable 2 cm below the costal margin. The extremities showed questionable swelling over both tibias and ankles, as well as tenderness to pressure over these areas. Urinalysis was within normal limits. The hemogram showed a leukocyte count of 14,800 with a normal differential. The hemoglobin was 12.0 gm per 100 ml, and hematocrit 31 per cent. There were many target cells and moderate hypochromia. Sickle cell preparation showed 30 per cent sickling. Fecal urobilinogen was 0.07 mg per 100 ml. Total serum bilirubin was 1.4 mg per 100

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ml, with 0.2 mg direct and 1.2 mg indirect. A bone marrow study showed moderate erythroid hyperplasia. Paper electrophoresis showed hemoglobin S-C.

The low grade fever subsided on the third day and all symptoms disappeared.

CASE 2

S. C., a 5½ year old negro girl, was first seen at the Children's Hospital Out Patient Department at the age of 18 months when she was hospitalized because of a febrile convulsion. A routine sickle cell preparation revealed 100 per cent sickling. She remained asymptomatic until 2 years of age, when she developed pain in both elbows during an upper respiratory infection. Since that time she had numerous visits to the Out Patient Department with respiratory infections and joint pains.

At the time of her last admission these pains were severe enough that she could not or would not stand up. She had been treated as an out patient for a recent episode of bronchopneumonia.

When admitted the patient was alert, co-operative and well oriented. Her pharynx was moderately injected. Her abdomen was slightly distended and the liver was palpated 2 cm below the right costal margin. The tip of the spleen was barely palpable. Her extremities showed no physical changes.

X-rays of the chest showed no evidence of disease. Urinalysis was essentially normal. Sickle cell preparation was reported as 50 per cent and 15 per cent sickling on two occasions. Hemogram on admission showed a hemoglobin of 10.5 gm per 100 ml, with hematocrit 30 per cent. The smear was described as showing anisocytosis, some polychromatic red blood cells and many target cells. There was a moderate leukocytosis with a shift to the left. A bone marrow smear showed evidence of active hematopoiesis. Bilirubin determinations ranged from a total of 1.8 mg per 100 ml (direct 0.4 mg and indirect 1.4 mg) on admission, to a total of 0.5 mg and 0.3 mg on two other occasions. Hemoglobin paper electrophoresis revealed the presence of hemoglobin S-C.

The patient was given chloramphenicol while studies were being done. She became afebrile and asymptomatic three days after admission. After several days she again showed evidence of infection, so antimicrobial therapy was resumed. During her hospitalization her leukocyte count returned to normal levels. It was also noted that the hemoglobin and hematocrit had made a steady but gradual decline to 7.5 mg per 100 ml, and 24 per cent respectively, but jaundice was never evident. She received a blood transfusion and was discharged in good condition. Follow-up visits have not revealed any return of joint symptoms in spite of several respiratory infections.

COMMENT

Case 1 represents a typical case of hemoglobin S-C disease with a mild compensated hemolytic syndrome, sickling of erythrocytes, large numbers of target cells, splenomegaly, and mild joint and abdominal complaints. These cases should and can be suspected clinically but can only be diagnosed by paper electrophoresis.

The second case represents a somewhat atypical case. The minimal to absent splenomegaly, the variable number of target cells, as well as the consistently falling hemoglobin and hematocrit would make one doubt the diagnosis of hemoglobin S-C disease were it not for the evidence of the hemoglobin electrophoresis.

The progressive anemia of this patient could represent the rare occurrence of a crisis or some other factor not adequately studied.

DISCUSSION

The combination of hemoglobin C with hemoglobin S usually produces a chronic, mild hemolytic syndrome which presents clinically with mild musculo-skeletal complaints and splenomegaly. Hematologically there are mild to moderate anemia, sickling of erythrocytes and large numbers of target cells.

Target cells may be found occasionally in normal individuals as well as under certain pathological conditions. In the Caucasian race they vary, normally comprising up to 3 per cent of total red cells, while up to 5 per cent may be found in the Negro race. Most authors report between 40 and 85 per cent target cells in hemoglobin S-C disease. The large number of these cells seems to be dependent on the presence of hemoglobin C. Other conditions which produce increased numbers of target cells are: 1) Sickle cell anemia and sickle cell trait, 2) Thalassemia major and minor, 3) Homozygous hemoglobin C, 4) Iron deficiency anemia, 5) Post hemorrhagic state, 6) Post splenectomy state, 7) Liver disease, 8) Dehydration, and 9) Steatorrhea.

Hemoglobin S which causes the erythrocytes to sickle is found in from 8–10 per cent of Negroes in the U. S. A., and one in forty of these will suffer from sickle cell anemia. The presence of hemoglobin C in the heterozygous and homozygous state has been estimated to occur in approximately 2 per cent of the Negro population.

The absence of sickling on blood smear or sickling preparation does not rule out the presence of hemoglobin S since sickling seems to be dependent on the amount of hemoglobin S present. Sickling does not appear with less than 7 to 10 per cent hemoglobin S.

The presence of the gene for hemoglobin C seems to potentiate the gene for hemoglobin S. This results in larger amounts of both of these abnormal hemoglobins than would be expected from a study of the amount of these hemoglobins in the parents having the S or C trait. Theoretically then, we could see typical S-C disease in the offspring of parents that show no sickling.

The anemia of S-C disease is usually mild, and is the result of a compensated hemolysis. The erythrocytes are normochromic and there is a slight reticulocytosis. The bone marrow shows active hematopoesis.

The musculo-skeletal complaints are usually referred to the abdomen and the joints. These are mild in nature and seldom require any treatment.

Splenomegaly of varying degrees is found in most cases and constitutes the outstanding physical finding in hemoglobin S-C disease.

Characteristically, the patient with hemoglobin S-C disease does not "perform his own medical splenectomy" as is the usual case in sickle cell anemia but splenomegaly persists into adult life. The presence of hemoglobin C seems to be responsible for the splenomegaly as this is also a prominent finding with homozygous hemoglobin C disease.

Crises are uncommon in this condition but may occur in infancy as well as in pregnancy. Vitreous hemorrhages and painless hematuria have been described as apparently due to hemoglobin S-C disease. Several cases of splenic infarction associated with high altitude flying have been associated with the presence of hemoglobin S-C.

At present the condition can be suspected clinically in the presence of sickling, mild anemia, splenomegaly, and large numbers of target cells; however, the diagnosis can be made with certainty only by hemoglobin electrophoresis.

Treatment should be symptomatic. Hospitalization is very seldom indicated and blood transfusions should not be used except very rarely in the most severe and intractable cases.

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RANULA OF WHARTON'S DUCT

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A mucous retention cyst located in the floor of the mouth and arising in a duct of the submaxillary or sublingual glands is known as a ranula. The ranula may be congenital or appear later in life. Potter[1] has reported ranulas in infants as young as three days and in the stillborn fetus as well.

The ranula is a slowly growing, soft, fluctuant, unilocular cystic lesion usually unilateral, and located in the floor of the mouth. It may sometimes disappear spontaneously or may persist until surgically removed. Large cysts may extend across the midline and appear to involve both sides. Histologically, the ranula is lined by large, pale, mucus-secreting cells. As the cyst enlarges the mucosa becomes thinner allowing the contained clear mucus to impart a bluish tinge.

The only subjective symptoms are due to the size of the tumor which raises the tongue and forces it posteriorly, and to the opposite side. This often interferes with mastication and speech, and may, in the very young, interfere with breathing.

In the operative removal of the ranula the entire cyst wall must be enucleated or marsupialized sufficiently so that the edges will not re-unite. Because the wall is thin and friable, complete dissection is often difficult. Large ranulas of the submaxillary duct are treated by marsupialization. The mucous membrane of the top of the cyst is excised down to the level of the floor of the mouth, permitting the lower part of the cyst to become the lining of the floor of the mouth. This method was reported by Bailey[2] (1931) and was quoted by Thoma and Brackett[3] who advised similar treatment. These authors added that suturing the margin of the cyst floor to the mucosa prevents closing over of the edges and reformation of the ranula. Ward[4] (1925) described a technique whereby the cyst lining is electrodesiccated following evacuation of the cyst content. Treatment of a large ranula involving the submaxillary duct usually results in the duct opening farther back in the mouth as the anterior portion is usually destroyed or partially cut away during treatment.

CASE REPORT

M. T., an 11 year old colored male, was seen in the Dental Clinic of the Out Patient Department of the Children's Hospital of D. C. on October 8, 1956. He complained of painful lip lesions and stated that he had had a recent toothache. His mother had noted a swelling under the tongue when he attempted to show her which tooth had been hurting.

The patient was in good health except for recurrent asthma.

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Upon examination, significant findings were confined to the oral cavity. Intra-oral examination disclosed caries of the permanent molars. A small vesicular lesion was present on the ventral surface of the tongue. It was not tender to palpation and the patient had not been aware of its presence. A non-tender swelling was noted to the right of the midline in the floor of the mouth. In the anterior portion of this mass the orifice of Wharton's duct was observed; posterior to this the mass appeared to embody the terminal part of the duct. The overlying mucosa had a pearl-like sheen. There were herpetic lesions on the upper and lower lips on the right side. Intra-oral radiograms were taken to determine the extent of caries, and the herpetic lesions were painted with one per cent merthiolate and three per cent camphorated oil to ease soreness. Sodium bicarbonate mouth rinses and a soft diet with plenty of fluids were prescribed.

On October 15, 1956, and November 1, 1956, the permanent molars were restored with chrome alloy crowns. The herpetic lesions were noted to be completely healed.

On November 9, 1956 an excision biopsy of the mass in the floor of the mouth was performed, using two per cent lidocaine hydrochloride with epinephrine 1:100,000 as local anesthesia. With blunt dissection, the distal portion of the mass was noted to extend into the substance of the duct, creating an orifice posterior to the previous Wharton opening. Three 6-0 silk sutures were placed along the incision line. The postoperative course was uneventful. Sutures were removed on November 13; the architecture of the floor of the mouth was intact and of normal contour. Pathology report was mucous retention cyst, submaxillary duct.

An excisional biopsy was performed on the tongue lesion on November 16, 1956; pathology report was sub-endothelial vesicle, ventral surface of the tongue.

No recurrence of either lesion has been noted to date.

DISCUSSION

Ranulas developing in childhood are comparatively infrequent in the experience of the authors. They respond favorably to surgical removal. Mere aspiration is not enough since their behavior is consistent with cystic processes occurring elsewhere in the body. Their painless development recalls the necessity of a thorough oral examination as a routine procedure in the examination of any patient.

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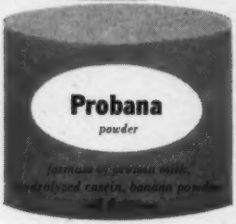

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